IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF OHIO
WESTERN DIVISION

LUANN PARKER,	)	Case No. C-1-00-766
	)	
Plaintiff,	)	Judge Susan J. Dlott
	)	
v.	)	
	)	
AVENTIS PASTEUR, INC., et al.	)	
	)	
	)	
Defendant.	)	

The following documents are Exhibits 1-4 to the deposition of David Griesemer taken on July 15, 2003.

CURRICULUM VITAE

Name: David A. Griesemer, M.D. **Birthdate:** [redacted]

Social Security #: [redacted]

Home Address: 1207 Southern Oak Way
Mt. Pleasant, SC 29466
Phone: 843/849-1474

Office Address: Medical University of SC
Department of Neurology
96 Jonathan Lucas Street
Charleston, SC 29425
Phone: 843/792-3224
Fax: 843/792-6995
Email: grieseda@musc.edu

Citizenship and/or Visa Information: USA

Education (beginning with Baccalaureate degree)

Institution/Location	Years	Degree/Date	Field of Study
Johns Hopkins University Baltimore, MD	1969-1972	BA/1972 Cum Laude	Human Biology
Johns Hopkins University School of Medicine Baltimore, MD	1972-1976	MD/1976	Medicine

Internship

Place	Dates
Johns Hopkins Hospital Baltimore, MD	1976-1977

Residency or Postdoctoral

Place	Dates
Johns Hopkins Hospital Baltimore, MD Assistant Resident in Pediatrics	1977-1978
University of Michigan Hospitals Ann Arbor, MI Child Neurology Fellow	1982-1985

Specialty/Board Certification

American Board of Psychiatry and Neurology
Neurology with Special Competence in Child Neurology
1992 (Certificate 821)

American Society of Neurorehabilitation
1993 (Certificate 376)

American Board of Psychiatry and Neurology
Clinical Neurophysiology
1997 (Certificate 828)

Licensure
Maryland (D19541), 1976-1993
Michigan (44935), 1982-1985
Arizona (15236), 1985-present
South Carolina (16681), 1993-present

Military Service
Active Duty
US Public Health Service
Keams Canyon, AZ
1978-1982

Active Reserves
US Air Force Reserve
Wurtsmith Air Force Base (SAC)
Luke Air Force Base (TAC
1982-1989

Faculty Appointments (begin with initial appointment)

Years	Rank	Institution	Department
1990-1993	Assistant Professor	University of Arizona College of Medicine Tucson, AZ	Pediatrics; Neurology
1993-1997	Assistant Professor	Medical University of South Carolina Charleston, SC	Neurology; Pediatrics
1997-2002	Associate Professor	Medical University of South Carolina Charleston, SC	Neurology; Pediatrics
2002-present	Tenure	Medical University of South Carolina Charleston, SC	Neurology; Pediatrics
2002-present	Professor	Medical University of South Carolina Charleston, SC	Neurology; Pediatrics

Administrative Appointments

Years	Position	Institution	Department
1980-1982	Director, Keams Canyon Indian Hospital	US Public Health Service Phoenix Area Indian Health Service Keams Canyon, AZ	N/A
1990-1993	Director, Pediatric Epilepsy Unit	Arizona Health Sciences Center Tucson, AZ	N/A
1990-1993	Medical Director	Fan Kane Research Fund For Brain-Injured Children Tucson, AZ	N/A
1992-1993	Medical Director Pediatric Rehab Program	Rehab Institute of Tucson Tucson, AZ	N/A
1993-2000	Director, Pediatric Epilepsy Program	Children's Hospital Medical University of SC Charleston, SC	N/A
1994-2000	Director, Clinical Neurophysiology Services	MUSC Hospital Charleston, SC	N/A
2000-present	Chairman, Department of Neurology	Medical University of SC Charleston, SC	Neurology
2000-present	Co-Director, Neuroscience Institute	Medical University of SC Charleston, SC	N/A

Hospital Appointments/Privileges

Active/Inactive	Institution
Inactive	Public Health Service Indian Hospital, Tucson, AZ
Inactive	Yavapai Regional Medical Center, Tuba City, AZ
Inactive	Public Health Service Indian Medical Center, Tuba City, AZ
Inactive	Children's Rehabilitation Services, Flagstaff, AZ
Inactive	Tucson Medical Center, Tucson, AZ
Inactive	University Medical Center, Tucson, AZ
Inactive	Desert Hills Neuropsychiatric Hospital, Tucson, AZ
Inactive	Children's Rehabilitation Services
Inactive	Square and Compass Children's Clinic, Tucson, AZ
	Rehab Institute of Tucson, Tucson, AZ
Active	Medical University of South Carolina, Charleston, SC
Inactive	Thad E. Saleeby Development Center, Hartsville, SC

Membership in Professional/Scientific Societies (including offices held)
Local
Charleston County Medical Society
National
American Academy of Cerebral Palsy and Developmental Medicine, elected member
American Academy of Neurology
American Academy of Pediatrics (Fellow), elected member
American Clinical Neurophsiology Society, elected member
American Epilepsy Society, elected member
American Society of Neurorehabilitation, elected member
Association for Research in Nervous and Mental Diseases, elected member
Child Neurology Society
Society for Neuroscience, elected member

International
Royal Society of Medicine (London), elected member

Editorial Positions
Johns Hopkins Medical Journal
Assistant Editor, 1974-1976

MedLink Neurology (Multimedia Internet and CD-ROM reference for Neurology
Associate Editor for Child Neurology, 1997-present

Emedicine: Neurology (Internet reference for neurology and pediatrics)
Associate Editor for Child Neurology, 1999-present

Extramural Grants/Award Amounts (current and past)
As Principal Investigator

1994-1996 Gabapentin pediatric monotherapy trial: a multicenter, double-blind, placebo-controlled, parallel group study in pediatric patients with benign childhood epilepsy with centrotemporal spikes.
Parke-Davis Research Foundation

1995-1998 An extended open-label gabapentin pediatric monotherapy trial following a double-blind study in pediatric patients with benign childhood epilepsy with centrotemporal spikes.
Parke-Davis Research Foundation

1995-1996 A double-blind parallel group comparison of gabapentin versus placebo as add-on therapy for epilepsy in children.
Parke-Davis Research Foundation

1995-1996 An open-label extension study of gabapentin in children with epilepsy who have participated in the double-blind study 945-186.
Parke-Davis Research Foundation

1995-1997 Efficacy and safety of oral adjunctive vigabatrin therapy compared to placebo in children with uncontrolled complex partial seizures: A parallel group study.
Hoescht Marion Roussel

Extramural Grants (Continued)

1996-1998 An open-label, follow-up, long-term maintenance study of vigabatrin as adjunctive therapy in children with uncontrolled complex partial seizures.
Hoescht Marion Roussel

1995-1996 Lamotrigine as add-on therapy in patients with a clinical diagnosis of Lennox-Gastaut syndrome (severe generalized epilepsy of childhood onset): a multicenter, double-blind, placebo controlled, parallel study.
Glaxo Wellcome Research & Development

1995-1996 An open-label study of Lamictal in patients who previously participated in a Lamictal pediatric trial.
Glaxo Wellcome Research & Development

1999-2000 Gabapentin pediatric add-on trial: A randomized, double-blind, placebo-controlled, parallel-group, multicenter study in patients with partial seizures.
Parke-Davis Pharmaceutical Research

1999-2000 Open-label, safety study of gabapentin as adjunct therapy in children aged 1 month through 4 years with seizures uncontrolled by current anticonvulsant drugs.
Parke-Davis Pharmaceutical Research

As Co-Investigator

1991-1993 Compassionate clearance protocol for the treatment of alternating hemiplegia of childhood with flunarizine
A. Rubens, MD (University of Arizona Health Sciences Center)
Janssen Research Foundation

1994-1997 Dynamical characterization of EEG signals during epileptic seizures In children
W. Schaffer, PhD, PI (Ecology and Evolutionary Biology, University of Arizona)

1999-present Learning impairments among survivors of childhood cancer
R. Mulhern, PhD, PI (St. Jude Children's Research Hospital)
R. Brown, PhD, Site PI (Medical University of South Carolina)
H. Frideman, MD, Site PI (Duke University Medical Center)

As Collaborator

2002-present Clinical biochemical and neurological correlates of autism
R. Michaelis, PhD, PI (JC Self Research Institute, Greenwood Genetic Center)

Intramural Grants/Award Amounts

As Principal Investigator

1992-1993 Language impairment in children with focal epileptic discharges
Biomedical Sciences Research Grant
University of Arizona College of Medicine

1994-1997 Electroconvulsive therapy for intractable seizures in children (HR#6244)
Medical University of South Carolina

1995-1996 Neurologic morbidity and development following elective circulatory arrest in infants (HR#6379)
Medical University of South Carolina

Intramural Grants (Continued)

1996 -1998 Determination of multi-modality evoked potentials at MUSC (HR#6641)
Medical University of South Carolina

1997-1999 Sleep disorders in children with epilepsy (HR#7215)
Medical University of South Carolina

As Co-Investigator

1997-2000 Lovastatin therapy for X-linked adrenoloeukodystrophy (HR#7210)
G. Shashidhar Pai, MD, PI
Medical University of South Carolina

As Collaborator

2000-2001 Learning impairments among survivors of childhood cancer) (HR#8351)
R. Brown, PhD, PI
Medical University of South Carolina

Awards/Honors/Membership in Honorary Societies

1980 Isolated Hardship Award
US Public Health Service
Keams Canyon, AZ

1987 Achievement Medal for Meritorious Service
US Air Force
Washington, DC

1992 Dean's Teaching Scholar
University of Arizona College of Medicine
Tucson, AZ

1993 Virginia Furrow Grant for Innovation in Medical Education
University of Arizona College of Medicine
Tucson, AZ

1993 Neurology Teaching Award
Department of Neurology
University of Arizona College of Medicine
Tucson, AZ

2000 Award of Tenure, College of Medicine
Medical University of South Carolina
Charleston, SC

2001 Jeffrey E. Gilliam Chair in Child Development
Medical University of South Carolina
Charleston, SC

Academic Committee Activities (past 5 years)

Medical University of South Carolina

Advisory Committee
Master of Science in Rehabilitation
College of Health Professions
1996-1998

Medical University of South Carolina (Committee Activities, continued)

Vice-Chairman
Executive Compliance Committee
Medical Executive Committee
University Hospital Medical Center
2000-2001

Board of Directors
University Medical Associates
2000-present

Executive Committee
Faculty Practice Plan
University Medical Associates
2001-present

Chair
Healthy Young and Development Workgroup
2002 Strategic Plan
2001-present

College of Medicine, Medical University of South Carolina

Freshman Curriculum Coordinating Committee
1997-2000

Clinical Core Rotations (Year III) Committee
Undergraduate Curriculum Committee
1999-2000

Co-Director
Neurology Core Curriculum
Course Evaluation Subcommittee
Undergraduate Curriculum Committee
1999-2001

Educational Policy Council
2000-present

Chairman
Medical Neurosciences (Year I) Steering Committee
2000-2001

Undergraduate Curriculum Committee
2001-present

Major Teaching Responsibilities (current)

Undergraduate Medical Education

Grader, Examination Questions in Neurology

Graduate Medical Education

Year I Medical Students
Lecturer, Clinical Correlations in Neuroscience
Medical Neuroscience Course

Coordinator, Neurologic Examination Sequence
Doctoring Curriculum

Year I-II Medical Students
Summer Health Professions Program
Amy Tu: "Neurologic morbidity in circulatory arrest in infants"
Thena Poteat: "Sleep disorders in children with epilepsy"

Mentor, Medical Campus Outreach
Venezuela – 1999, 2000
Year III Medical Students
Lecturer
Core Neurology Rotation

Mentor, Pediatric Neurology Clinic
Core Neurology Rotation

Mentor, Pediatric Neurology Consult Service
Core Neurology Rotation

Examiner, Final Oral Examination
Core Neurology Rotation

Year IV Medical Students
Mentor, Senior Neurology Research Elective
Kristen Jerger: "Non-linear dynamics in epileptic seizures"
Elaine Moreland: "Topiramate for intractable seizures"

Pediatric Residents
Mentor, Pediatric Neurology Clinic (Required Neurology Rotation)
Mentor, Pediatric Neurology Consult Service (Required Neurology Rotation)
Mentor, Epilepsy Monitoring Service
Pediatric Specialty Inpatient Service

Neurology Residents
Mentor, Pediatric Epilepsy Clinic (Required Pediatric Rotation)
Mentor, Pediatric Neurology Clinic (Required Pediatric Rotation)
Mentor, Pediatric Neurology Consult Service (Required Pediatric Rotation)
Mentor, Pediatric EEG Interpretation
Lecturer, Epilepsy and EEG Conferences

Clinical Neurophysiology Fellows
Supervisor, Pediatric EEG Interpretation
Supervisor, Video EEG Interpretation
Supervisor, ICU EEG in Intraoperative EP Monitoring
Mentor, Pediatric Epilepsy Clinic

Sleep-Clinical Neurophysiology Fellow
Mentor, Adult and Pediatric Sleep Clinics, 1998-1999

Child Psychiatry Fellow
Mentor, Pediatric Neurology Clinic

Nursing Staff
Supervisor, Pediatric Neurology protocols
Clinical Nurse Specialist (Georgette Smith, MSN)
Inservice Education (Neuroscience and Pediatric nurses)

Continuing Medical Education

Graduate Medical Education
Lecturer, Management of Neurologic Disorders
Lecturer, to various physician groups throughout South Carolina

Continued Medical Education
Neurology Grand Rounds, weekly participation and yearly presentation
CME Conferences in Neurology

Major Clinical Interests and Responsibilities

Responsibility

Developing a dynamic Department of Neurology with both clinical and pre-clinical components

Interests

Neuropsychiatric disorders (autism, attention disorders, compulsive tic disorders)
CNS inflammation as a cause of epilepsy in children
Forensic neuropediatrics

Selected Lectures/Presentations

International

"Understanding Epilepsy"
College of Medicine, University of the Andes
Merida, Venezuela
June 2000

Other

Recurring presentations at
Frontiers in Pediatrics
South Carolina Neurological Association
Kiawah Epilepsy Conference
South Carolna Epilepsy Foundation Annual Conference
MUSC Clinical Neuroscience Symposia

Extramural Professional Activities
American Academy of Neurology
Residency Inservice Examination Subcommittee
1998-2001

Child Neurology Society
Practice Committee
1999-present

South Carolina Epilepsy Foundation
Board of Directors
1999-present

Community Service
Public School Board
Keams Canyon, AZ
1980-1982

School Board
Palmetto Christian Academy
Mt. Pleasant, SC
1994-1998

Publications
Peer Reviewed Journal Articles

1. Griesemer DA, Winkelstein JA, Luddy R. Pneumococcal meningitis in major sickle hemoglobinopathy. *J Pediatr* 1978;92:82-84.

2. Griesemer DA, Barton LL, Reese CM, Johnson PC, Gabrielson JAB, Talwar D, Visvesara GS. Amebic meningoencephalitis caused by *Balamuthia mandrillaris*. *Pediatr Neurol* 1994;10:249-254.

3. Griesemer DA, Theodorou AA, Berg RA, Spera TD. Local fibrinolysis in a child with cerebral venous thrombosis. *Pediatr Neurol* 1994;10:78-80.

4. Talwar D, Baldwin MB, Hutzler R, Griesemer DA. Epileptic spasms in older children: persistence beyond infancy. *Epilepsia* 1995;36:151-155.

5. Griesemer DA. Pergolide in the treatment of Tourette syndrome. *J Child Neurol* 1997;12:402-403.

6. Griesemer DA, Kellner CH, Beale MD, Smith GM. Electroconvulsive therapy for treatment of intractable seizures: Initial findings in two children. *Neurology* 1997;49:1389-1392.

7. Holden KR, Clarke SL, Griesemer DA. Long-term outcomes of conventional therapy for infantile spasms. *Seizure* 1997;6:201-205.

8. Motte J, *et al.* Lamotrigine for generalized seizures associated with the Lennox-Gastaut Syndrome. *NEJM* 1997;337:1807-1812.

9. Anderson DL, Spratt EG, Macias MM, Jellinek MS, Murphy JM, Pagano M, Griesemer DA, Holden KR, Barbosa E. Use of the pediatric symptom checklist in the pediatric neurology population. *Pediatr Neurol* 1999;20:116-120.

10. Anderson DL, Spratt EG, Macias MM, Jellinek MS, Murphy JM, Pagano M, Griesemer DA, Holden KR, Barbosa E. Use of the Pediatric Symptom Checklist in the pediatric neurology population. *Pediatr Neurol* 1999;20:116-120.

11. Moreland EC, Griesemer DA, Holden KR. Topiramate for intractable childhood epilepsy. *Seizure* 1999;8:38-40.

12. Helmers SL, Griesemer DA, Dean JC, Sanchez JD, Labar D, Murphy JV, Park YD, Shuman RM, Morris GL. Observations on the use of vagus nerve stimulation earlier in the course of pharmacoresistant epilepsy: patients with seizures for six years or less. *Neurologist* (in press).

Non-peer Reviewed Publications

1. Griesemer DA , Johnston MV. Kainate-induced seizures alter calcium channel antagonist binding. *Ann Neurol* 16;178:1984.

2. Griesemer DA , Baldwin MA. Visuopsychic dyskinesia. *Ann Neurol* 1992;32:443-444.

3. Griesemer DA, Talwar D, Hadden RO, Johnson MI, Baldwin MA. Reflex apnea with autonomic dysynergy (RAAD). *Epilepsia* 1993;34(Supplement 6):43.

4. Talwar D, Baldwin MA, Griesemer DA. Epileptic spasms in older children: Persistence beyond infancy. *Epilepsia* 1993; 34(Supplement 6):37.

5. Griesemer DA, Baldwin MA. Munchausen-by-proxy epilepsy in foster families. *Epilepsia* 1994; 35(Supplement 8):56.

6. Griesemer DA, Kayser HG. Language impairments and seizure disorders. *American Electroencephalographic Society*, 1994.

7. Talwar D, Weinand ME, Baldwin MA, Labiner DM, Griesemer DA, Oomen KJ. Surgical treatment of intractable symptomatic occipital epilepsy. *Epilepsia* 1994;35(S8):69.

8. Lookadoo SE, Holden KR, Griesemer DA. Felbamate therapy in childhood-onset epilepsy. *Epilepsia* 1995;36(Supplement 4):5.42.

9. Spratt EG, Anderson D, Pagano M, Richardson S, Jellinek M, Murphy JM, Griesemer D, Edwards EJ, Macias M. Comorbidity of pediatric neurologic disorders and psychosocial function. *American Academy of Child and Adolescent Psychiatry,* 1995.

10. Spratt E, Anderson D, Macias M, Pagano M, Jellinek M, Griesemer D, Holden K, Barbosa E. Comorbidity of psychiatric and language disorders in pediatric neurology. *American Academy of Child and Adolescent Psychiatry*, 1997.

11. Moreland EC, Griesemer DA, Holden KR. Topiramate: A timely AED for intractable childhood epilepsy? *Epilepsia* 1997;38(Supplement 8):193-194.

12. Anderson DL, Spratt EG, Macias MM, Murphy JM, Pagano M, Griesemer DA, Holden, KR, Barbosa E. Use of the pediatric symptom checklist in the pediatric neurology population. *Fifth International Congress of Behavioral Medicine, Copenhagen,* 1998.

13. Burgeois B, Brown LW, Pellock JM, Buroker M, Greiner M, Garofalo EA, Schimschock JR, Griesemer DA, Bebin ME, Murphy JV, The Gabapentin BECTS Study Group. Gabapentin (Neurontin) monotherapy in children with benign childhood epilepsy with centrotemporal spikes

(BECTS): A 36-week, double-blind, placebo-controlled study. *Epilepsia* 1998;39(Supplement 6):163.

14. Messenheimer JA, Haynie CJ, Risner ME, Lamictal US 41 Pediatric Study Group: Long-term tolerability of Lamictal in pediatric patients. *Epilepsia* 1998;39(Supplement 6):51-52.

15. Spratt EG, Anderson DL, Macias M, Jellinek M, Holden KR, Griesemer D, Barbosa E: Collaborative screening of psychiatric and language disorders in pediatric neurology clinics. *Eleventh Annual Research Conference, Louis de la Parte Florida Mental Health Institute, Tampa*, 1998.

Chapters in Scholarly Books and Monographs

1. Griesemer DA. Muscular dystrophy. In: *Griffith's 5 Minute Clinical Consult,* (Dambro MR, Griffith J, eds), Williams-Wilkins/Philadelphia PA, 1995:690-691; 1996:690-691; 1997:698-699; 1998:700-701.

2. Spratt EG, Anderson D, Pagano M, Macias M, Jellinek M, Murphy M, Griesemer D, Holden K, Barbosa. Collaborative screening of psychiatric and language disorders in pediatric neurology. In: *The 11th Annual Research Conference Proceedings, A System of Care for Children's Mental Health: Expanding the Research Base* (Willis J, Liberton C, Kutash K, Friedman R, eds), Tampa: University of South Florida, The Louis de la Parte Florida Mental Health Institute, Research and Training Center for Children's Mental Health, 1999.

3. Griesemer DA, Waheed N. Muscular dystrophy. In *Griffith's 5 Minute Clinical Consult,* (Dambro MR, eds), Lippincott Williams & Wilkins/Philadelphia PA, 2000, 2001.

Peer-reviewed Electronic Publications

1. Griesemer DA. Neonatal meningitis. In: *eMedicine Neurology,* (Lorenzo NY, ed), eMedicine.com/St. Petersburg FL, 2001.

2. Griesemer DA. Lead. In: *eMedicine Neurology,* (Lorenzo NY, ed), eMedicine.com/St. Petersburg FL, 2001.

Non-peer Reviewed Electronic Publications

1. Griesemer DA. Focal cortical dysplasia. In: *Neurobase* (Gilman S, Goldstein G, Waxman S, eds), Arbor Publishing Corp/La Jolla, CA, 1995.

2. Griesemer DA. Acute hemiplegia of childhood. In: *Neurobase* (Gilman S, Goldstein G, Waxman S, eds), Arbor Publishing Corp/La Jolla CA, 1995, 1997.

3. Griesemer DA. Craniosynostosis. In: *Neurobase* (Gilman S, Goldstein G, Waxman S, eds), Arbor Publishing Corp/La Jolla, CA, 1995, 1997.

4. Griesemer DA. Incontinentia pigmenti. In: *Neurobase* (Gilman S, Goldstein G, Waxman S, eds), Arbor Publishing Corp/La Jolla CA, 1995, 1997.

5. Griesemer DA. Hemimegalencephaly. In: *Neurobase* (Gilman S, Goldstein G, Waxman S, eds), Arbor Publishing Corp/La Jolla CA, 1995, 1998.

6. Griesemer DA. Cerebral venous thrombosis in infants and children. In: *Neurobase* (Gilman S, Goldstein G, Waxman S, eds), Arbor Publishing Corp/La Jolla CA, 1997.

7. Griesemer DA. Breath-holding spells. In: *Neurobase* (Gilman S, Goldstein G, Waxman S, eds), Arbor Publishing Corp/La Jolla CA, 1998.

8. Griesemer DA. Opsoclonus-myoclonus syndrome. In: *Neurobase* (Gilman S, Goldstein G, Waxman

S, eds), Arbor Publishing Corp/La Jolla CA, 1995, 1998.

9. Griesemer DA. Tuberous sclerosis complex. In: Gilman S. *Neurobase*. (Gilman S, Goldstein G, Waxman S, eds), Arbor Publishing Corp/San Diego CA, 1999.

10. Holden KR, Griesemer DA. Neurologic complications of congenital heart disease. In: *Neurobase* (Gilman S, eds), Arbor Publishing Corp/San Diego CA, 1999.

11. Steedman J, Griesemer D. Mental retardation. In: *Neurobase*. (Gilman S), Arbor Publishing Corp/San Diego CA, 1999.

12. Griesemer DA. Childhood lead poisoning. In: *MedLink-Neurobase* (Gilman S, eds, Arbor Publishing Corp/San Diego CA, 2001.

13. Griesemer DA, Carter TD. Acute hemiplegia in childhood. In: *MedLink-Neurobase*, (Gilman S, ed), Arbor Publishing Corp/San Diego CA, 2001.

14. Griesemer DA, Hutchison K. Incontinentia pigmentia. In: *MedLink Neurology*, (Gilman S, ed), MedLink Corp/San Diego, 2001.

15. Griesemer DA, Koury DW. Opsoclonus-myoclonus syndrome. In: *MedLink Neurology,* (Gilman S, ed), MedLink Corp/San Diego CA, 2001.

16. Griesemer DA, Mushtaq R. Tuberous sclerosis complex. In: *MedLink Neurology,* (Gilman S, ed), MedLink Corp/San Diego CA, 2001.

17. Griesemer DA, Pitman GM. Cerebral venous thrombosis in infants and children. In: *MedLink Neurology,* (Gilman S, ed), MedLink Corp/San Diego CA, 2001.

18. Griesemer DA, Sobczak JM. Craniosynostosis. In: *MedLink Neurology,* (Gilman S, ed), MedLink Corp/San Diego CA, 2001.

19. Griesemer DA, Williams TJ. Hemimegalencephaly. In: *MedLink Neurology,* (Gilman S, ed), MedLink Corp/San Diego CA, 2001.

20. Steedman JG, Weinstein B, Miller G, Griesemer DA. Mental retardation. In: *MedLink Neurology,* (Gilman S, ed), MedLInk Corp/San Diego CA, 2001.

21. Turner RP, Griesemer DA. Breath-holding spells. In: *MedLink Neurology* (Gilman S, ed), MedLink Corp/San Diego CA, 2001.

22. Griesemer DA, Li M. Muscular dystrophy. In: *Griffith's 5 Minute Clinical Consult* (Dambro M, ed), Lippincott Williams & Wilkins/Philadelphia PA, 2002.

Other

1. Griesemer DA. A Textbook of Epilepsy, by Laidlaw and Richens [book review]. *Johns Hopkins Med J* 1977; 141:301
2. Griesemer DA. Mammalian Parenting: Biochemical, Neurobiological and Behavioral Determinants, (Krasnegor NA, Bridges RS, ed) [book review]. *JAMA* 1991;265:1033.
3. Griesemer DA, Johnson MI. Guillain-Barre syndrome and plasmapharesis in childhood [letter]. *Ann Neurol* 1991;29:688.
4. Griesemer DA. The case of Rebecca Montoya (Opsoclonus-myoclonus syndrome). *DxR* [interactive computer-based case study]. Carbondale IL, DxR Development Group, 1994.

LuAnn Parker
DOB 1/18/46
DOE 10/10/98

ATTORNEY WORK PRODUCT
Do Not Copy

PMH:
- hypertension since pregnancy in 1986, Rx'd with Procardia, Tenormin, Catapress
- diabetes in 4/93; started on Glucatrol
- migraine in 12/93 with normal CT on 12/5/93
- obesity in 8/96 at 210 lb; on Redux for 2 mo; resumed 6/97

FH: 23-yr-old son at Miami University, 12-year-old daughter; recently retired teacher

Medications at injury: Midrin, clonidine, glucotrol

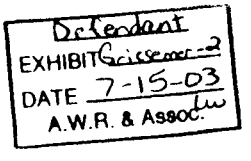
Flu shot on 10/10/98 (Saturday)
- 10/12 awoke with pain in neck and occiput and dizziness
- 10/13 seen in ER, pain moved to right periorbital area, numbness over hands >> body, some difficulty thinking (didn't roll down window at Wendy's, couldn't turn into driveway); CT non-focal
- 10/14 evaluated by neurologist Marvin Rorick: sluggish thinking, difficult putting on underwear; good balance but "slightly unsteady in Romberg position"; MRI showed bilateral posterior parietal enhancement, primarily meningeal in location; in addition there were multiple small nodular areas in deep white matter of parietal lobe
- 10/15 increased headache with numbness of arms and legs, impaired perception, increased dizziness
- hard time "starting and stopping," falling to the left, positive Romberg

- hospitalized 10/21 – 10/25, apraxia of dressing, turning into driveway
  - On 10/22 CSF protein 28, glucose 169,1 WBC; IgG 1.3, oligoclonal bands absent, myelin basic protein
  - Seizure inferred by post-ictal state, transferred to MICU
  - Started insulin sliding scale
  - Proprioceptive deficits
  - Non-epileptiform EEG

- hospitalized 10/27 – 11/9, increasing ataxia with titubation, but afebrile; decreased sensation for urination (uninhibited voiding patter), but using timed voiding
  - medications: started on dexamethasone 4 mg q6 hr, insulin, glipizide, antihypertensives
  - WESR 10, ANCA, herpes simplex ½ IgM < 1:10, HIV ½ nonreactive
  - 10/30 brain MRI: unchanged, multiple small nodular non-enhancing areas of high signal intensity in the deep white matter of both parietal lobes; small nodular enhancing lesions in high parietal regions bilaterally also unchanged; diminution of irregular enhancement of parietal meninges; however, clinically patient had better position sense of left arm and decreased vertigo
  - 11/2 cervical MRI: normal; lumbar MRI: degenerative facet disease with mild stenosis and mild disc bulge at L3-4
  - increased numbness of lips, and increased ataxia when sitting led to 11/4 exam by Flenner (PM&R): euphoric, left arm and leg 4+/5 with slightly decreased coordination, abnormal sensation neck to waist; reports no taste, smell, sense of full bladder
  - began steroid taper on 11/6

- Decadron decreased from BID to QD on 11/11, but symptoms worsened and dose resumed on 11/13

- Left leg pain and swelling began around 11/10, and hospitalized 11/14 for DVT of superficial femoral and popliteal vein
  - dexamethosone decreased from 4 mg to 2 mg BID



- 12/8/98 Decadron decreased to 2 qAM and 4 qPM

- 12/25/98 ER visit for "her dead mother was in the room shaking her body"; on sliding scale insulin, Glucatrol, clonidine, Atenolol, Procardia, coumadin, dexamethsone 2 mg – 4 mg, lorazepam, B12, glutathione, Antivert, Midrin, vitamin E, elderberry extract, Darvocet, acidophilus, Keflex for UTI

- admitted 12/26 with BP 170/104, FBS 263 mg/dl, glucose 418
  - Hypokalemia 2.8, hypogammaglobulinemia 2° steroids
  - ANA 1:40, RPR nonreactive
  - Thrombocytopenia with platelets 93K on 12/26 and 51 K on 12/29
  - 12/28 MRI: new small focus of high signal with irregular enhancement in right frontal parietal region, and progressive white matter disease in corona radiata bilateraly compared to 10/28

- transferred to Cleveland Clinic 12/29/98 – 1/5/99
  - mild weakness L .> R, narrow-based gait, no ataxia, tandem with mild difficulty; no hyperreflexia
  - 12/31 cerebral angiogram – no vasculitis
  - paraneoplastic anti Hu and anti Yo negative; WESR 59; negative cardiolipin antibodies; normal homocysteine, normal lactate:pyruvate, negative lupus panel; negative ANA, ds DNA
  - platelets 74K; CRP elevated at 6.4
  - normal CNS protein 24, IgG synthesis, negative VDRL
  - 1/4 organic psychosis with manic component, secondary to steroids, cerebral atrophy, menopause, social stressors, discharged on valproate, risperidol
- 2/1/99 ADEM stable, but not quite back to cognitive baseline; continues on VPA, risperidone
- 10/1/99 "appears to be at baseline"

Diagnoses

- post-vaccination ADEM, associated with
  - visual-spatial impairment / apraxia
  - left hemiparesis
  - loss of proprioceptive sense and sensory ataxia
- acute confusional state with auditory hallucinations, fixed delusions, agitation, possibly secondary to
  - steroid therapy
  - ADEM
- type II diabetes mellitus, insulin-dependent secondary to steroid therapy
- heterozygous for Factor V Leiden with deep vein thrombosis
- idiopathic thrombocytopenic purpura
- hypertension x 12 years
- migraine headaches

3

AFFIDAVIT

Charleston County, South Carolina

David A. Griesemer, M.D., being under oath or affirmation, says:

1. I am a physician licensed to practice medicine in the states of Arizona and South Carolina.

2. I am board certified in the following fields: 1) Neurology with Special Competence in Child Neurology and 2) Clinical Neurophysiology.

3. I have attached as part of this affidavit, my Curriculum Vitae.

4. I have reviewed the medical, hospital and other records of Ms. Luann Parker.

5. In my review of Ms. Luann Parker's records I found the following:

a. Ms. Parker, was administered an intermuscular injection of Influenza virus vaccine known as FLUZONE®, on October 10, 1998.

b. Ms. Parker was free of neurological illness or impairment prior to October 12, 1998.

c. On October 12, 1998, following this flu vaccine injection, she developed a severe headache, ataxia, vertigo and tingling in her hands.

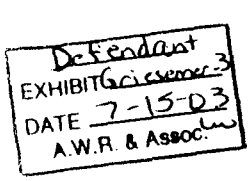
d. On October 12, 1998, Ms. Parker awoke with pain in her neck and occiput and with dizziness.

e. On October 13, 1998, with complaints of numbness in her hands, some difficulty in thinking and with more severe headaches, Ms. Parker was taken by ambulance to the emergency room of Bethesda North Hospital.

f. On October 14, 1998, Dr. Brewer, her primary care physician, referred Ms. Parker to Marvin Rorick, M.D., a neurologist.

g. On October 15, 1998, she underwent an MRI examination; the finding of the MRI showed bilateral posterior parietal enhancement, primarily meningeal in location, with additional, multiple small nodular areas in the deep white matter, which were not enhancing.

h. Dr Rorick noted in a letter to Dr. Brewer: "This appears to be a mild disequilibrium syndrome which may represent a postvaccination effect."



i. Ms. Parker was admitted to Bethesda North Hospital on October 21, 1998, with a diagnosis of "acute cerebritis" and a secondary diagnosis of "post influenza vaccine reaction."

j. On October 21, 1998, Dr. Rorick, wrote a neurology note that states in part: "Patient is 52 Year old lady in good health until week of 10/12/98, within 48 hours of receiving a flu shot at Thriftway in Blue Ash on 10/10. Initial symptoms unsteady gait, numbness in both hands, headache mainly [r] sided."

k. On October 25, 1998, Ms. Parker was discharged from Bethesda North Hospital to home, with a principal diagnosis of "encephalitis following immunization procedures."

l. Ms. Parker was again admitted to Bethesda North Hospital on October 27, 1998 for increasing ataxia with titubation and an uninhibited voiding problem; the meningeal enhancement on the MRI during this admission was decreasing. The principal diagnosis explaining her admission was "Post Flu shot Cerebritis."

m. Silvania Ng, M.D. a neurologist saw Ms. Parker as a consultant on October 29, 1998; Dr. Ng, reported in her assessment: "Plan: Severe ataxia, Status post flu shot. I did contact the CDC and have talked to Dr. Carolyn Briiges, one of the doctors responsible for the bunch of flu vaccine, and she states that this whole picture could be secondary to the flu shot although is very rare such report . . . "

n. Ms. Parker was discharged from the hospital November 9, 1998.

o. Ms. Parker was again admitted on November 14, 1998 as an inpatient to Bethesda North Hospital with a primary admitting diagnosis of "probable deep vein thrombosis of the LT leg." Ms. Parker was discharged from the hospital on November 17, 1998.

p. On December 25, 1998, Ms. Parker went the Emergency Room of Bethesda North Hospital with a chief complaint of hearing voices; she was stabilized and then released.

q. The psychotic behavior continued, and on December 26, 1998 Ms. Parker was admitted to Bethesda North Hospital with an admitting diagnosis was acute confusional state; during this hospitalization on December 28, 1998, Ms. Parker underwent another MRI; there was a finding of a new small focus of high signal on this MRI, with irregular enhancement in the right frontal-parietal region, with progressive white matter disease in the corona radiata bilaterally when compared to the October 28, 1998 study.

r. On December 29, 1998, Ms. Parker was transferred to the Cleveland Clinic

Foundation Hospital, under Dr. M. May's care; during this hospitalization, there was a thorough attempt to rule out other problems causing her neurological symptoms.

s. Ms. Parker was discharged to her home from the Cleveland Clinic on January 5, 1999, with the principal diagnosis of: "Acute Demyelinating Encephalomyelitis."

6. Based upon my review of Luann Parker's records, I state that within a reasonable degree of medical and scientific certainty, that her symptoms associated with ADEM (Acute disseminated encephalomyelitis) were caused by her vaccination received in October of 1998. Furthermore, additional symptoms associated with steroid treatment of ADEM, represent secondary effects following the vaccination.

WITNESS affiant's signature on this 16th day of September, 2002

David A. Griesemer MD

{Signature of affiant}

Sworn and subscribed before me a notary public in and for the County of Charleston, State of South Carolina on this 16th day of September, 2002.

Maria C. Kingston

My Commission Expires May 12, 2003

A.H.F.S. Category 80:12

Rx only

Influenza Virus Vaccine USP Trivalent Types A and B (Zonal Purified, Subvirion) 1998-99 Formula – For 6 Months and Older

Fluzone®

SPECIAL NOTICE: *FOR USE IN IMMUNIZATION BY OR UNDER THE DIRECTION OF A PHYSICIAN.*

Caution: Federal (USA) law prohibits dispensing without prescription.

DESCRIPTION

Fluzone®, Influenza Virus Vaccine USP, (Zonal Purified, Subvirion) for intramuscular use, is a sterile suspension prepared from influenza viruses propagated in chicken embryos. The virus-containing fluids are harvested and inactivated with formaldehyde. Influenza virus is concentrated and purified in a linear sucrose density gradient solution using a continuous flow centrifuge. The virus is then chemically disrupted using Polyethelene Glycol p-Isooctylphenyl Ether (Triton® X-100 – A registered trademark of Rohm and Haas, Co.) producing a "split-antigen." The split-antigen is then further purified by chemical means and suspended in sodium phosphate-buffered isotonic sodium chloride solution. Fluzone has been standardized according to USPHS requirements for the 1998-99 influenza season and is formulated to contain 45 micrograms (µg) hemagglutinin (HA) per 0.5 mL dose, in the recommended ratio of 15 µg HA each, representative of the following three prototype strains: A/Beijing/262/95 (H1N1), A/Sydney/05/97 (H3N2) and B/Harbin/07/94 (a B/Beijing/184/93-like strain).[1] Gelatin 0.05% is added as a stabilizer and thimerosal (mercury derivative) 1:10,000 is added as a preservative. Fluzone, after shaking syringe/vial well, is essentially clear and slightly opalescent in color.

ANTIBIOTICS ARE NOT USED IN THE MANUFACTURE OF FLUZONE.

CLINICAL PHARMACOLOGY

Influenza A viruses are classified into subtypes on the basis of two surface antigens: hemagglutinin (H) and neuraminidase (N). Three subtypes of hemagglutinin (H1, H2, H3) and two subtypes of neuraminidase (N1, N2) are recognized among influenza A viruses that have caused widespread human disease. Immunity to these antigens – especially to the hemagglutinin – reduces the likelihood of infection and lessens the severity of disease if infection occurs. Infection with a virus of one subtype confers little or no protection against viruses of other subtypes. Furthermore, over time, antigenic variation (antigenic drift) within a subtype may be so marked that infection or vaccination with one strain may not induce immunity to distantly related strains of the same subtype. Although influenza B viruses have shown more antigenic stability than influenza A viruses, antigenic variation does occur. For these reasons, major epidemics of respiratory disease caused by new variants of influenza continue to occur. The antigenic characteristics of circulating strains provide the basis for selecting the virus strains included in each year's vaccine.[1]

Formal subclassification utilizing neuraminidase antigens has not been done for influenza B viruses.

Influenza illness is characterized by abrupt onset of fever, myalgia, sore throat, and nonproductive cough. Unlike other common respiratory illnesses, influenza can cause severe malaise lasting several days. More severe illness can result if either primary influenza pneumonia or secondary bacterial pneumonia occurs. During influenza epidemics, high attack rates of acute illness result in both increased numbers of visits to physicians' offices, walk-in clinics, and emergency rooms and increased hospitalizations for management of lower-respiratory-tract complications.[1,2]

Elderly persons and persons with underlying health problems are at increased risk for complications of influenza infection. If they become ill with influenza, such members of high-risk groups (see Groups at Increased Risk for Influenza-Related Complications under Target Groups for Special Vaccination Programs) are more likely than the general population to require hospitalization. During major epidemics, hospitalization rates for persons at high-risk may increase substantially, depending on the age group. Previously healthy children and younger adults also may require hospitalization for influenza-related complications, but the relative increase in their hospitalization rates during epidemics is less than for persons who belong to high-risk groups. Estimated rates of influenza-associated hospitalization have varied substantially in studies of different influenza epidemics occurring from 1972 through 1981:

- Rates for persons greater than or equal to 65 years of age (all of whom are considered to be in a high-risk group) have ranged from approximately 200 to greater than 1,000 per 100,000 population.[1]
- Rates for persons 45 to 64 years of age have ranged from approximately 80 to 400 per 100,000 population for those with high-risk medical conditions and from approximately 20 to 40 per 100,000 for those without high-risk conditions.[1]
- Rates for persons 15 to 44 years of age have ranged from approximately 40 to more than 60 per 100,000 population for those with high-risk conditions and from approximately 20 to 30 per 100,000 population for those without high-risk conditions.[1]
- Rates for children 5 to 14 years of age have ranged from approximately 200 per 100,000 population for those with high-risk conditions to 20 per 100,000 population for those without high-risk conditions.[1]
- Rates for children 0 to 4 years of age have ranged from approximately 500 per 100,000 population for those with high-risk conditions to 100 per 100,000 population for those without high-risk conditions.[1]

During influenza epidemics from 1969-70 through 1993-94, the estimated number of influenza-associated hospitalizations has ranged from approximately 20,000 to more than 300,000 per epidemic, with an average of approximately 130,000 to 170,000 per epidemic. The greatest numbers of influenza-associated hospitalizations have occurred during epidemics caused by type A(H3N2) viruses, with an estimated average of 160,000 to 200,000 excess hospitalizations per epidemic.[1]

Increased mortality results not only from influenza and pneumonia but also from cardiopulmonary and other chronic diseases that can be exacerbated by influenza. In studies of influenza epidemics occurring from 1972-73 through 1994-95, excess deaths associated with influenza occurred during 19 of 23 influenza epidemics. During those 19 influenza seasons, estimated rates of influenza-associated deaths ranged from approximately 25 to greater than 150 per 100,000 persons greater than 65 years of age, who account for more than 90% of the deaths attributed to pneumonia and influenza. An estimate of greater than 20,000 influenza-associated deaths occurred during each of 11 different US epidemics from 1972-73 through 1994-95, and greater than 40,000 influenza-associated deaths occurred during each of six of these 11 epidemics.[1]

Pneumonia and influenza deaths may be increasing because the number of elderly persons in the US population is increasing, as well as the number of persons less than 65 years of age at increased risk for influenza-related complications (e.g., organ-transplant recipients, neonates in intensive-care units, and persons who have cystic fibrosis and acquired immunodeficiency syndrome [AIDS], all of whom have longer life expectancies than in previous years).[1]

Vaccinating persons at high-risk each year before the influenza season is currently the most effective measure for reducing the impact of influenza. Vaccination can be highly effective when it is a) directed at persons who are most likely to experience complications or who are at increased risk for exposure and b) administered to persons at high-risk during hospitalizations or routine health-care visits before the influenza season, thus making special visits to physicians' offices or clinics unnecessary. When vaccine and epidemic strains of virus are well matched, achieving high vaccination rates among persons living in closed settings (e.g., nursing homes and other chronic-care facilities) can reduce the risk for outbreaks of influenza by inducing herd immunity.[1]

Other indications for vaccination include the desire to avoid becoming ill with influenza, reduce the severity of disease, or reduce the chance of transmitting influenza to close contacts who are members of high-risk groups.[1]

Each year's influenza vaccine contains three virus strains (usually two type A and one type B) representing the influenza viruses that are likely to circulate in the United States in the upcoming winter. The vaccine is made from highly purified, egg-grown viruses that have been made noninfectious (inactivated). Influenza vaccine rarely causes systemic or febrile reactions. Whole-virus and subvirion preparations are available.[1]

Most vaccinated children and young adults develop high post-vaccination hemagglutination-inhibition antibody titers. These antibody titers are protective against illness caused by strains similar to those in the vaccine or the related variants that may emerge during outbreak periods. Elderly persons and persons with certain chronic diseases may develop lower post-vaccination antibody titers than healthy young adults and may remain susceptible to influenza-related upper-respiratory-tract infection. However, even if such persons develop influenza illness despite vaccination, the vaccine can be effective in preventing lower-respiratory-tract involvement or other secondary complications, thereby reducing the risk for hospitalization and death.[1]

The effectiveness of influenza vaccine in preventing or attenuating illness varies, depending primarily on the age and immunocompetence of the vaccine recipient and the degree of similarity between the virus strains included in the vaccine and those that circulate during the influenza season. When a good match exists between vaccine and circulating viruses, influenza vaccine has been shown to prevent illness in approximately 70% to 90% of healthy persons less than 65 years of age. In these circumstances, studies also have indicated that the effectiveness of influenza vaccine in preventing hospitalization for pneumonia and influenza among elderly persons living in settings other than nursing homes or similar chronic-care facilities ranges from 30% to 70%.[1]

Among elderly persons residing in nursing homes, influenza vaccine is most effective in preventing severe illness, secondary complications, and death. Studies of this population have indicated that the vaccine can be 50% to 60% effective in preventing hospitalization and pneumonia and 80% effective in preventing death, even though efficacy in preventing influenza illness may often be in the range of 30% to 40% among the frail elderly. Achieving a high rate of vaccination among nursing home residents and staff can reduce the spread of infection in a facility, thus preventing disease through herd immunity. Vaccination of health care workers in nursing homes also has been demonstrated to reduce the impact of influenza among residents.[1]

INDICATIONS AND USAGE

Fluzone is indicated only for immunization against the selected virus strains contained in the vaccine (see **PRECAUTIONS** section).

Influenza vaccine (subvirion) is strongly recommended for any person greater than or equal to 6 months of age who – because of age or underlying medical condition – is at increased risk for influenza complications. Health-care workers and others (including household members) in close contact with persons in high-risk groups also should be vaccinated. In addition, influenza vaccine may be administered to any person who wishes to reduce the chance of becoming infected with influenza.[1]

Dosage recommendations for the 1998-99 season are given in Table 1. Guidelines for the use of vaccine among certain patient populations are given below.[1]

Although the current influenza vaccine can contain one or more of the antigens administered in previous years, annual vaccination using the current vaccine is necessary because immunity declines in the year following vaccination.[1]

REMAINING 1997-98 VACCINE SHOULD NOT BE USED TO PROVIDE PROTECTION FOR THE 1998-99 INFLUENZA SEASON.[1]

Persons at high-risk who are seen by health-care providers for routine care or as a result of hospitalization should be offered influenza vaccine as early as September. (See Foreign Travelers section for foreign travel exceptions.) The optimal time for organized vaccination campaigns for persons in high-risk groups is usually the period from October through mid-November. In the United States, influenza activity generally peaks between late December and early March. High levels of influenza activity infrequently occur before December. Administering vaccine too far in advance of the influenza season should be avoided in facilities such as nursing homes, because antibody levels might begin to decline within a few months of vaccination. Vaccination programs can be undertaken as soon as current vaccine is available if regional influenza activity is expected to begin earlier than December.[1]

Vaccine should be offered to both children and adults up to and even after influenza virus activity is documented in a community.[1]

Two doses administered at least one month apart may be required for satisfactory antibody responses among previously unvaccinated children less than 9 years of age; however, studies of vaccines similar to those being used currently have indicated little or no improvement in antibody response when a second dose is administered to adults during the same season.[1]

During recent decades, data on influenza vaccine immunogenicity and side effects have been obtained for intramuscularly administered vaccine. Because recent influenza vaccines have not been adequately evaluated when administered by other routes, the intramuscular route is recommended. Adults and older children should be vaccinated in the deltoid muscle and infants and young children in the anterolateral aspect of the thigh.[1]

TARGET GROUPS FOR SPECIAL VACCINATION PROGRAMS
To maximize protection of high-risk persons, they and their close contacts should be selected for organized vaccination programs.[1]

Groups at Increased Risk for Influenza-Related Complications:[1]
- Persons greater than or equal to 65 years of age
- Residents of nursing homes and other chronic-care facilities that house persons of any age with chronic medical conditions
- Adults and children with chronic disorders of the pulmonary or cardiovascular systems, including children with asthma
- Adults and children who have required regular medical follow-up or hospitalization during the preceding year because of chronic metabolic diseases (including diabetes mellitus), renal dysfunction, hemoglobinopathies, or immunosuppression (including immunosuppression caused by medications)
- Infants, children and teenagers (6 months to 18 years of age) who are receiving long-term aspirin therapy and therefore might be at risk for developing Reye syndrome after influenza[1,3,4]
- Women who will be in the second or third trimester of pregnancy during the influenza season

Also, persons who smoke tobacco products are at increased risk for influenza-related complications and therefore should receive influenza vaccine.[5,6,7]

Groups That Can Transmit Influenza to Persons at High-Risk:[1]
Persons who are clinically or subclinically infected can transmit influenza virus to persons at high risk that they care for or with whom they live. Some persons at high-risk (e.g., the elderly, transplant recipients, and persons with AIDS) can have a low antibody response to influenza vaccine. Efforts to protect these members of high-risk groups against influenza might be improved by reducing the likelihood of influenza exposure from their care givers. Therefore, the following groups should be vaccinated:

- physicians, nurses, and other personnel in both hospital and outpatient-care settings;
- employees of nursing homes and chronic-care facilities who have contact with patients or residents;
- providers of home care to persons at high-risk (e.g., visiting nurses and volunteer workers); and
- household members (including children) of persons in high-risk groups.

General Population
Physicians should administer influenza vaccine to any person who wishes to reduce the likelihood of becoming ill with influenza (the vaccine can be administered to children as young as 6 months of age). Persons who provide essential community services should be considered for vaccination to minimize disruption of essential activities during influenza outbreaks. Students or other persons in institutional settings (e.g., those who reside in dormitories) should be encouraged to receive vaccine to minimize the disruption of routine activities during epidemics.[1]

Pregnant Women
Influenza-associated excess mortality among pregnant women has not been documented except during the pandemics of 1918-1919 and 1957-1958. However, because death-certificate data often do not indicate whether a woman was pregnant at the time of death, similar studies conducted during interpandemic periods may underestimate the impact of influenza in this population. Case reports and limited studies suggest that pregnancy may indeed increase the risk for serious medical complications as a result of increases in heart rate, stroke volume and oxygen consumption, decreases in lung capacity and changes in immunologic function. A recent study of the impact of influenza during 17 interpandemic influenza seasons found that the relative risk of hospitalization for selected cardiorespiratory conditions among pregnant women increased from 1.4 during weeks 14 to 20 of gestation to 4.7 during weeks 37 to 42 when their hospitalization rates were compared with rates among women who were 1 to 6 months post-partum. The risk during the third trimester was comparable to the risk for non-pregnant women with high-risk medical conditions for whom influenza vaccine has traditionally been recommended. It was estimated that immunizing 1,000 women who would be in their third trimester during influenza season would prevent one hospitalization[8]

In view of these and other data which suggest that influenza infection may cause increased morbidity in women during the second and third trimesters of pregnancy, the ACIP recommends that health-care workers who provide care for pregnant women should consider administering influenza vaccine.[1] **(Refer to Pregnancy Category C statement.)**

Breastfeeding Mothers
Influenza vaccine does not affect the safety of breastfeeding for mothers or infants. Breastfeeding does not adversely affect immune response and is not a contraindication for vaccination.[1]

Persons Infected with Human Immunodeficiency Virus (HIV)
Limited information exists regarding the frequency and severity of influenza illness among HIV-infected persons, but reports suggest that symptoms might be prolonged and the risk for complications increased for some HIV-infected persons. Influenza vaccine has produced protective antibody titers against influenza in vaccinated HIV-infected persons who have minimal AIDS-related symptoms and high CD4+ T-lymphocyte cell counts. In patients who have advanced HIV disease and low CD4+ T-lymphocyte cell counts, however, influenza vaccine may not induce protective antibody titers; a second dose of vaccine does not improve the immune response for these persons.[1]

Recent studies have examined the effect of influenza vaccination on replication of HIV type 1 (HIV-1). Although some studies have demonstrated a transient (i.e., 2- to 4-week) increase in replication of HIV-1 in the plasma or peripheral blood mononuclear cells of HIV-infected persons after vaccine administration, other studies using similar laboratory techniques have not indicated any substantial increase in replication. Deterioration of CD4+ T-lymphocyte cell counts and progression of clinical HIV disease have not been demonstrated among HIV-infected persons who receive vaccine. Because influenza can result in serious illness and complications and because influenza vaccination may result in protective antibody titers, vaccination will benefit many HIV-infected patients.[1]

Foreign Travelers
The risk for exposure to influenza during foreign travel varies, depending on season and destination. Because of the short incubation period for influenza, exposure to the virus during travel can result in clinical illness that begins while traveling, which is an inconvenience or potential danger, especially for persons at increased risk for complications. Persons preparing to travel to the tropics at any time of year or to the southern hemisphere from April through September should review their influenza vaccination histories. If they were not vaccinated the previous fall or winter, they should consider influenza vaccination before travel. Persons in the high-risk categories should be especially encouraged to receive the current vaccine. Persons at high-risk who received the previous season's vaccine before travel should be revaccinated in the fall or winter with the current vaccine.[1]

SIMULTANEOUS ADMINISTRATION OF OTHER VACCINES, INCLUDING CHILDHOOD VACCINES
CONCURRENT USE WITH PNEUMOCOCCAL VACCINE. Fluzone has been shown in clinical studies to be acceptable for concurrent use with pneumococcal vaccine using separate syringes at different sites. Although Influenza Virus Vaccine is recommended in certain patients for annual use, the pneumococcal vaccine should only be given once.[1,8,9]

Children at high-risk for influenza-related complications can receive influenza vaccine at the same time they receive other routine vaccinations, including pertussis vaccine (DTaP or DTP) using separate syringes at different sites. Because influenza vaccine can cause fever when administered to young children, DTaP[9] (which is less frequently associated with fever and other adverse events) is preferable.

CONTRAINDICATIONS
INFLUENZA VIRUS IS PROPAGATED IN EGGS FOR THE PREPARATION OF INFLUENZA VIRUS VACCINE. THEREFORE, FLUZONE SHOULD NOT BE ADMINISTERED TO ANYONE WITH A HISTORY OF HYPERSENSITIVITY (ALLERGY), ESPECIALLY ANAPHYLACTIC REACTIONS, TO EGGS OR EGG PRODUCTS. IT IS ALSO A CONTRAINDICATION TO ADMINISTER FLUZONE TO INDIVIDUALS KNOWN TO BE SENSITIVE TO THIMEROSAL. EPINEPHRINE INJECTION (1:1000) MUST BE IMMEDIATELY AVAILABLE SHOULD AN ACUTE ANAPHYLACTIC REACTION OCCUR DUE TO ANY COMPONENT OF FLUZONE.

Fluzone should not be administered to patients with acute respiratory or other active infections or illnesses.

Immunization should be delayed in a patient with an active neurologic disorder, but should be considered when the disease process has been stabilized.

WARNINGS
This product contains dry natural latex rubber as follows: The stopper to the vial contains dry natural latex rubber. In the case of the syringe, the needle cover contains dry natural latex rubber, but the plunger for the syringe contains no rubber of any kind.

Fluzone should not be administered to individuals who have a prior history of Guillain-Barré syndrome (GBS).

If Fluzone is administered to immunosuppressed persons, the expected antibody response may not be obtained.

As with any vaccine, vaccination with Fluzone may not protect 100% of susceptible individuals.

PRECAUTIONS
GENERAL
Care is to be taken by the health-care provider for the safe and effective use of this vaccine.

EPINEPHRINE INJECTION (1:1000) MUST BE IMMEDIATELY AVAILABLE SHOULD AN ACUTE ANAPHYLACTIC REACTION OCCUR DUE TO ANY COMPONENT OF THIS VACCINE.

Influenza virus is remarkably capricious in that significant antigenic changes may occur from time-to-time. *It is known definitely that Influenza Virus Vaccine, as now constituted, is not effective against all possible strains of influenza virus. Protection is afforded most people only against those strains of virus from which the vaccine is prepared or against closely related strains.*

During the course of any febrile respiratory illness or other active infection, use of Influenza Virus Vaccine should be delayed.

Since the likelihood of febrile convulsions is greater in children 6 months through 35 months of age, special care should be taken in weighing relative risks and benefits of vaccination.

Prior to an injection of any vaccine, all known precautions should be taken to prevent side reactions. This includes a review of the patient's history with respect to possible sensitivity to the vaccine or similar vaccine, to possible sensitivity to dry natural latex rubber, previous immunization history, current health status (see **CONTRAINDICATIONS** and **WARNINGS** sections) and a knowledge of the current literature concerning the use of the vaccine under consideration.

Special care should be taken to prevent injection into a blood vessel.

A separate, sterile syringe and needle or a sterile disposable unit should be used for each patient to prevent transmission of hepatitis or other infectious agents from person to person. Needles should not be recapped and should be disposed of according to biohazard waste guidelines.

INFORMATION FOR PATIENT
Patients, parents or guardians should be fully informed by their health-care provider of the benefits and risks of immunization with Influenza Virus Vaccine.

Patients, parents or guardians should be instructed to report any serious adverse reactions to their health-care provider.

Drug Interaction:
Although influenza vaccination can inhibit the clearance of warfarin, theophylline, phenytoin, and aminopyrine therapy, studies have failed to show any adverse clinical effects attributable to these drugs in patients receiving influenza vaccine.[9,11,12,13,14,15,16]

If Fluzone is administered to immunosuppressed persons or persons receiving immunosuppressive therapy, the expected antibody response may not be obtained. This includes patients with asymptomatic HIV infection, AIDS or AIDS-Related Complex, severe combined immunodeficiency, hypogammaglobulinemia, or aggammaglobulinemia; altered immune states due to diseases such as leukemia, lymphoma, or generalized malignancy; or an immune system compromised by treatment with corticosteroids, alkylating drugs, antimetabolites or radiation.[17]

PREGNANCY
REPRODUCTIVE STUDIES – PREGNANCY CATEGORY C
Animal reproduction studies have not been conducted with Influenza Virus Vaccine USP Trivalent, Types A and B. It is not known whether Influenza Virus Vaccine can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Influenza Virus Vaccine should be given to a pregnant woman only if clearly needed (see **INDICATIONS AND USAGE** section).

PEDIATRIC USE
SAFETY AND EFFECTIVENESS OF FLUZONE (SUBVIRION) IN INFANTS BELOW THE AGE OF 6 MONTHS HAVE NOT BEEN ESTABLISHED.

ADVERSE REACTIONS
Because influenza vaccine contains only noninfectious viruses, it cannot cause influenza Respiratory disease after vaccination represents coincidental illness unrelated to influenza vaccination. The most frequent side effect of vaccination is soreness at the vaccination site that lasts up to 2 days. These local reactions generally are mild and rarely interfere with the ability to conduct usual daily activities.

Two types of systemic reactions have occurred:
- Fever, malaise, myalgia, and other systemic symptoms can occur following vaccination and most often affect persons who have had no exposure to the influenza virus antigens in the vaccine (e.g., young children). These reactions begin 6 to 12 hours after vaccination and can persist for 1 or 2 days. Recent placebo-controlled trials suggest that in elderly persons and healthy young adults, split-virus influenza vaccine is not associated with higher rates of systemic symptoms (e.g., fever, malaise, myalgia, and headache) when compared with placebo injections.[1]
- Immediate – presumably allergic – reactions (e.g., hives, angioedema, allergic asthma, and systemic anaphylaxis) occur rarely after influenza vaccination. These reactions probably result from hypersensitivity to some vaccine component; the majority of reactions are most likely related to residual egg protein. Although current influenza vaccines contain only a small quantity of egg protein, this protein can induce immediate hypersensitivity reactions among persons who have severe egg allergy. Persons who have developed hives, have had swelling of the lips or tongue, or have experienced acute respiratory distress or collapse after eating eggs should consult a physician for appropriate evaluation to help determine if vaccine should be administered. Persons who have documented immunoglobulin E(IgE)-mediated hypersensitivity to eggs – including those who have had occupational asthma or other allergic responses due to exposure to egg protein – also might be at increased risk for reactions from influenza vaccine, and similar consultation should be considered.[1,10,11,12,13,14,15,16]

The protocol for influenza vaccination developed by Murphy and Strunk may be considered for patients who have egg allergies and medical conditions that place them at increased risk for influenza-associated complications.[1,18]

Although the 1976 swine influenza vaccine was associated with an increased frequency of Guillain-Barré syndrome (GBS), evidence for a causal relationship of GBS with subsequent vaccines prepared from other virus strains is less clear.[1,19,20,21] However, obtaining strong evidence for a possible small increase in risk is difficult for a rare condition such as GBS, which has an annual background incidence of only 10 to 20 cases per million adults. During three of four influenza seasons studied from 1977 through 1991, the point estimates of the overall relative risks of GBS after influenza vaccination were slightly elevated; but were not statistically significant in any of these studies. However, a recent study of the 1992-93 and 1993-94 seasons, investigators found an elevation in the overall relative risk for GBS of 1.83 (95% Confidence Interval =1.12 to 3.00) during the 6 weeks following vaccination, representing an excess of an estimated 1 to 2 cases of GBS per million persons vaccinated; the combined number of GBS cases peaked 2 weeks after vaccination. The increase in the relative risks and the increased number of cases in the second week after vaccination may be the result of vaccination but also could be the result of other factors (e.g., confounding or diagnostic bias) rather than a true vaccine-related risk.[1]

Among persons who received the swine influenza vaccine in 1976, the rate of GBS that exceeded the background rate was slightly less than 10 cases per million persons vaccinated. Even if GBS were a true side effect in subsequent years, the estimated risk for GBS of 1 to 2 cases per million persons vaccinated is substantially less than that for severe influenza, which could be prevented by vaccination in all age groups, especially persons greater than or equal to 65 years of age and those who have medical indications for influenza vaccination. During different epidemics occurring from 1972 through 1981, estimated rates of influenza-associated hospitalization have ranged from approximately 200 to 300 hospitalizations per million population for previously healthy persons 5 to 44 years of age and from 2,000 to greater than 10,000 hospitalizations per million population for persons greater than or equal to 65 years of age. During epidemics from 1972-73 through 1994-95, estimated rates of influenza-associated deaths have ranged from approximately 300 to greater than 1,500 per million persons greater than or equal to 65 years of age, who account for more than 90% of all influenza-associated deaths. The potential benefits of influenza vaccination clearly outweigh the possible risks for vaccine-associated GBS.[1]

The average case-fatality ratio for GBS is 6% and increases with age. However, no evidence indicates that the case-fatality ratio for GBS differs among vaccinated persons and those not vaccinated.[1]

Whereas the incidence of GBS in the general population is very low, persons with a history of GBS have a substantially greater likelihood of subsequently developing GBS than persons without such a history. Thus, the likelihood of coincidently developing GBS after influenza vaccination is expected to be greater among persons with a history of GBS than among persons with no history of this syndrome. Whether influenza vaccination might be causally associated with this risk for recurrence is not known.[1]

Neurological disorders temporally associated with influenza vaccination such as encephalopathy, optic neuritis, partial facial paralysis, and brachial plexus neuropathy have been reported. However, no cause and effect has been established.[22,25] Almost all persons affected were adults, and the described clinical reactions began as soon as a few hours and as late as 2 weeks after vaccination. Full recovery was almost always reported.[24,26,26]

Reporting of Adverse Events
Reporting by patients, parents or guardians of all adverse events occurring after vaccine administration should be encouraged. Adverse events following immunization with vaccine should be reported by the health-care provider to the US Department of Health and Human Services (DHHS) Vaccine Adverse Event Reporting Systems (VAERS). Reporting forms and information about reporting requirements or completion of the form can be obtained from VAERS through a toll-free number 1-800-822-7967.[27]

The health-care provider also should report these events to the Director of Medical Affairs, Connaught Laboratories, Inc., a Pasteur Mérieux Connaught Company, Route 611, PO Box 187, Swiftwater, PA 18370 or call 1-800-822-2463.

DOSAGE AND ADMINISTRATION
Parenteral drug products should be inspected visually for particulate matter and/or discoloration prior to administration whenever solution and container permit. If either of these conditions exist, the vaccine should not be administered.

The syringe/vial should be well shaken before withdrawing each 0.5 mL dose.

Do NOT inject intravenously.

Injections of Influenza Virus Vaccine should be administered intramuscularly, preferably in the region of the deltoid muscle, in adults and older children. The preferred site for infants and young children is the anterolateral aspect of the thigh. Before injection, the skin over the site to be injected should be cleansed with a suitable germicide. After insertion of the needle, aspirate to assure that the needle has not entered a blood vessel.

Influenza vaccine should be offered beginning in September (see **INDICATIONS AND USAGE** section).

Children less than 9 years of age who have not previously been vaccinated should receive two doses of vaccine at least one month apart to maximize the likelihood of a satisfactory antibody response to all three vaccine antigens. The second dose should be administered before December, if possible.[1]

Fluzone (Subvirion) is to be used for persons 6 months of age and older. Fluzone (Subvirion) is NOT approved for infants under 6 months of age. The dosage is as follows:

TABLE 1[1] – Influenza Vaccine Dosage by Age Group
1998 – 1999 Season

Age Group	Vaccine†	Dosage	No. of Doses
6 – 35 months	Split virus only	0.25 mL	1 or 2*
3 – 8 years	Split virus only	0.50 mL	1 or 2*
9 – 12 years	Split virus only	0.50 mL	1
> 12 years	Whole or split virus	0.50 mL	1

† Because of the lower potential for causing febrile reactions, only split-virus (subvirion) vaccines should be used for children. Immunogenicity and side effects of split- and whole-virus vaccines are similar among adults when vaccines are administered at the recommended dosage.

* Two doses administered at least one month apart are recommended for children less than 9 years of age who are receiving influenza vaccine for the first time.

HOW SUPPLIED

Syringe, 0.5 mL. (Shake syringe well before administering.) **(Do not use for administering 0.25 mL.)** – Product No. 49281-362-11

Vial, 5 mL, for administration with needle and syringe (NOT to be used with jet injector). (Shake vial well before withdrawing each dose.) – Product No. 49281-362-15

STORAGE

Store between 2° – 8°C (35° – 46°F). Potency is destroyed by freezing. **DO NOT USE FLUZONE IF IT HAS BEEN FROZEN.**

REFERENCES

1. Recommendations of the Advisory Committee on Immunization Practices (ACIP). Prevention and control of influenza. MMWR 47: No. RR-6, 1998
2. Feigin RD, et al. Textbook of Pediatric Infectious Diseases. (Second Edition) Saunders: 1709-1729, 1987
3. CDC. Update: Influenza Activity-Micronesia, United States. MMWR 35: 685-687, 1986
4. CDC. Reye Syndrome-United States, 1985. MMWR 35: 66-74, 1986
5. Mulloy E. Management of Chronic Obstructive Pulmonary Disease. Ir Med J Vol 89 (6): 202, 204, 1996
6. Zimmerman RK, et al. Adult immunizations – a practical approach for clinicians: Part II. Am Fam Physician 51 (4): 859-867, 1995
7. Rothbarth PH, et al. Sense and nonsense of influenza vaccination in asthma and chronic obstructive pulmonary disease. Am J Respir Crit Care Med 151: 1682-1686, 1995
8. ACIP. Pneumococcal polysaccharide vaccine. MMWR 38: 64-76, 1989
9. DeStefano F, et al. Simultaneous administration of influenza and pneumococcal vaccines. JAMA 247: 2551-2554, 1982
10. Renton KW, et al. Decreased elimination of theophylline after influenza vaccination. Can Med Assoc J 123: 288-290, 1980
11. Fischer RG, et al. Influence of the trivalent influenza vaccine on serum theophylline levels. Can Med Assoc J 126: 1312-1313, 1982
12. Lipsky BA, et al. Influenza vaccination and warfarin anticoagulation. Ann Intern Med 100: 6: 835-837, 1984
13. Kramer P, et al. Effect of influenza vaccine on warfarin anticoagulation. Clin Pharmacol Ther Vol 35, #3: 416-418, 1984
14. Patriarca PA, et al. Influenza vaccination and warfarin or theophylline toxicity in nursing-home residents. New Engl J Med 308: 1601-1602, 1983
15. Levine M, et al. Increased serum phenytoin concentration following influenza vaccination. Clin Pharm 3: 505-509, 1984
16. Kilbourne ED. Inactivated Influenza Vaccines. Effects of influenza vaccination on drug metabolism. Vaccines (Plotkin and Mortimer eds.) Saunders Company: 429, 1988
17. ACIP. Immunization of children infected with human T-lymphotropic virus type III/lymphadenopathy-associated virus. MMWR 35: 595-606, 1986
18. Murphy KR, et al. Safe administration of influenza vaccine in asthmatic children hypersensitive to egg proteins. J Pediatr 106: 931-933, 1985
19. Schonberger LB, et al. Guillain-Barré syndrome following vaccination in the National Influenza Immunization Program, United States, 1976-1977. Am J Epid 110: 105-123, 1979
20. Schonberger LB, et al. Guillain-Barré Syndrome: Its epidemiology and associations with influenza vaccination. Ann Neurol 9 (Suppl.): 31-38, 1981
21. Kurland LT, et al. Swine influenza vaccine and Guillain-Barré syndrome. Epidemic or artifact? Arch Neurol, Vol 42, 1089-1090, 1985
22. CDC. Adverse Events Following Immunization. Surveillance Report No. 3, 1985-1986, Issued February 1989
23. Data on file, Connaught Laboratories, Inc.
24. Barry DW, et al. Comparative trial of influenza vaccines. II. Adverse reactions in children and adults. Am J Epid 104: 47-59, 1976
25. Retaillaiu HF, et al. Illness after influenza vaccination reported through a nationwide surveillance system, 1976-1977. Am J Epid III (3): 270-278, 1980
26. Guerrero IC, et al. No increased meningoencephalitis after influenza vaccine. N Engl J Med 300 (10): 565, 1979
27. CDC. Vaccine Adverse Event Reporting System – United States. MMWR 39: 730-733, 1990

Product information
as of May 1998

Manufactured by:
CONNAUGHT LABORATORIES, INC.
Swiftwater, Pennsylvania 18370, USA

Printed in USA

PASTEUR MÉRIEUX CONNAUGHT
RHÔNE-POULENC GROUP

3755/3756

5